PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	19.11.2004
Applicant's or agent's file reference JAF/PG5019	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/12161	30.10.2003	01.11.2002

Applicant
GLAXO GROUP LIMITED

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the International preliminary examining authority:

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference JAF/PG5019	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/12161	International filing date *(day/month/year)* 30.10.2003	Priority date *(day/month/year)* 01.11.2002
International Patent Classification (IPC) or both national classification and IPC C07C275/28		
Applicant GLAXO GROUP LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07.05.2004	19.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Seelmann, M Telephone No. +49 89 2399-8335

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/12161

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-43 as originally filed

Claims, Numbers

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 8

   because:

   ☒ the said international application, or the said claims Nos. 8 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7,9-14
	No:	Claims	8
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	8

2. Citations and explanations

   see separate sheet

The present application relates to phenylethanolamine derivatives of formula (I) (claims 1-7), preparation (claim 14), medical uses (claims 8-10, 13) and pharmaceutical composition (claims 10-12) thereof.

Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III.1 The structural parameter R^{21} is not defined in claim 1. Preferred embodiments of this parameter listed on page 6, lines 18-25 in the description do not allow to provide an accurate definition, since R^{15} represents hydrogen, halogen or C_{1-4} alkyl. Accordingly options comprising the structural parameter should be removed from the present application for reasons of clarity about the sought scope of protection.

III.2 According to Rule 67.1 (iv), the present authority did examine claim 8 in the light of the technical effects of the claimed compounds, since its subject-matter is directed to a method of treatment of the human or animal body.

Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1 WO 03 072 539 P-document
D2 WO 02 070 490
D3 GB 2 159 151

V.1 Novelty

All documents **D1** to **D3** relate to phenylethanolamine derivatives as agonists of β-adrenoreceptors and useful in the treatment of respiratory diseases. The compounds disclosed in all three documents differ from the presently claimed in that they fall into the proviso of the present application, i.e. $R^{14} = (CH_2)_pOR^{18}$, q = 1 and R^{16} = OH and additionally those of **D2** correspond to $R^1 = XNR^6CONR^7R^8$ with R^8 forming a bond with X so that the free urea is not disclosed or the cycle disclosed is not condensed with the phenyl ring (**D2**, claim 1, cases (d) or (f)).

Novelty is accordingly recognized for the different subject-matters of the present

application.

V.2 Inventive step

The subject-matters of claims 1-14 do not fulfill the requirements of Article 33(3) PCT for the following reasons:

The closest state of the art for the present application is represented by **D2**. **D2** discloses structurally similar compounds which do not fall under the present application because of only R^1. In the present application, such a structural variation is alleged to lead to derivatives with the same qualitative properties as those described in **D2**. In view of the experimental part and the other information as given in the description, it can be assumed that this problem has been solved for those compounds, wherein Ar1 = (ii) or (ii) (page 6 of the description), preferred embodiments of cases (a) and (b) of claim 1; R^{16} = OH; R^{17} = H; R^{14}= CH_2OH or NH-COH; R^3-R^5 = H; m = 5; n = 4; R^2 = H, Me; R^1 = NH-CO-NHR' with R' = H, Pyr, ϕ; p = 0.

a) The structural modification of the claimed compounds from those of **D2**, R^1, is that they correspond to the uncyclized urea group or the one condensed with the phenyl ring and not the non-condensed one. If the man skilled in the art should recognize an inventive step for such a structural modification on the basis that it is not obvious then further definitions as described in claim 1 cannot also be considered as obvious. Therefore an iventive could only be acknowledged for a reasonable generalisation of the examples 1-4 or claim 7. Every generalisation of the examples, however, would not be allowed under Article 34(2)b) EPC.

b) The problem underlying the present application cant be seen in the provision of further novel derivatives. In view of the extremely close structural relationship to **D2** compounds (condensed *versus* non-condensed urea group), it is considered that the man skilled in the art would have obviously expected the same qualitative properties shown by the compounds of **D2** also for the present compounds. **D3** supports such expectation, since in this document claim 1 englobes compounds posessing a phenyl substituted with an free urea group (**D3**, claim 1, NR^5COR^6 with R^6 being NR^3R^4). The proposed solution is an obvious alternative in view of the teachings of **D2** and **D3**. Therefore, the problem underlying the present application should be seen in the provision of new derivatives having unexpected properties over those of the closest prior art compounds (**D2**). In the absence of comparative test results or other appropriate information it is not possible to decide whether such a problem has been

solved or not. In the case where comparative tests are envisaged in order to support an inventive step, these must be carried out between the compounds of the present application having the maximum structural similarity with the compounds of the closest prior art, such that the effect is shown to have its origins in the distinguishing feature of the claimed invention.

V.3 Industrial applicability

For the assessment of the present claim 8 on the question whether it is industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.